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Slower reacquisition after partial extinction in human contingency learning

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Abstract

Extinction is a very relevant learning phenomenon from a theoretical and applied point of view. One of its most relevant features is that relapse phenomena often take place once the extinction training has been completed. Accordingly, as extinction-based therapies constitute the most widespread empirically validated treatment of anxiety disorders, one of their most important limitation is this potential relapse. We provide the first demonstration of relapse reduction in human contingency learning using mild aversive stimuli. This effect was found after partial extinction (i.e., reinforced trials were occasionally experienced during extinction, Experiment 1) and progressive extinction treatments (Experiment 3), and it was not only due to differences in uncertainty levels between the partial and a standard extinction group (Experiment 2). The theoretical explanation of these results, the potential uses of this strategy in applied situations, and its current limitations are discussed.

Keywords: Extinction, contingency learning, relapse, aversive learning

Learning relationships between different events relevant to organisms is ubiquitous, and takes place almost constantly (Clark, 2013; Friston, 2003). Most of the time, this acquired knowledge is helpful, as it is the basis of useful predictions about future events or inferences about their relationships. However, it can also be maladaptive. For example, in many anxiety disorders, seemingly harmless cues may become associated to strong and disruptive emotional responses, leading to distress and daily problems for those suffering them (Beckers, Krypotos, Boddez, Effting, & Kindt, 2013; Mineka & Zinbarg, 2006).

Fortunately, this type of learning is flexible in the sense that, once it has been acquired, it may be modified or altered. One of the ways in which this modification can take place is through extinction, the repeated presentation of a given cue in the absence of the consequences with which it had been previously associated (Pavlov, 1927). A progressive reduction in the acquired response to this cue is observed after experiencing a series of presentations of the cue alone. This flexibility allows the organism not only to adapt to changes in the cue-outcome relationships as they occur in the environment but also to ease those maladaptive forms of learning that lead to disruptive emotional responses. For example, in cognitive and behavioral therapies of anxiety disorders, exposure therapy -a repeated, systematic, and controlled exposure to the feared cue, in the absence of any traumatic event- seems to be a key component to success (Bouton, 2002, Longmore & Worrell, 2007; Norton & Price, 2007). Unfortunately, extinction is not such a robust effect as acquisition itself, and several factors can lead to a recovery of the original fear response, or relapse. Thus, the current challenge is not so much to achieve the fear reduction but to prevent its relapse (Vervliet, Craske, & Hermans, 2013). The return of fear was first documented by Rachman (1966) in relation to the reemergence of fear following systematic desensitization. In the existing literature, estimates of return of fear after exposure therapy range from 19% to 62% according to the review by Craske and

Mystkowski (2006). Thus, relapse may be considered as a serious difficulty for cognitive behavioral therapy of anxiety disorders. In the present series of experiments we will focus on how certain forms of relapse can be attenuated in the case of a human contingency learning paradigm (see Shanks, 2010, for a review of the contingency learning literature).

There are various sources of relapse that may take place after behavioral extinction (Bouton, 2002, 2004 or Vervliet et al., 2013 for reviews), affecting both responses acquired in the laboratory and fear responses suffered by patients with anxiety disorders. One of these forms of relapse described in the literature is rapid reacquisition (Ricker & Bouton, 1996). Rapid reacquisition refers to the effect that, after extinction, if the cue is again paired with the outcome with which it was previously associated, this new learning is faster than the original learning, indicating a carry-over effect of the original learning.

Interestingly, some other forms of relapse such as renewal, reinstatement or spontaneous recovery have been evidenced in animal as well as human conditioning studies, using different experimental paradigms, and also following exposure therapy in clinical settings (Craske, Liao, Brown, & Vervliet, 2012). Relapse phenomena, then, have been regarded as providing a useful insight into the nature of extinction and its underlying mechanisms. For a start, all the effects show that responding to a seemingly extinguished cue can reappear under certain conditions, suggesting that extinction does not erase previous learning. Instead, it seems that extinction implies a new learning that may be expressed or not depending on additional factors. Understanding both extinction and relapse has been the focus of interest of much research as it would provide essential information to understand extinction mechanisms as well as sound basis to improve exposure based therapies (see Milad & Quirk, 2012 or Vervliet et al., 2013 for recent reviews).

A fruitful research heuristic is that provided by theoretical accounts of extinction and its related phenomena. Currently, the model proposed by Mark Bouton (Bouton, 1993, 2002) is the most widely accepted explanation of these effects. According to Bouton's model, the extinction treatment produces a new learning, separate from the original one. A new inhibitory association between the conditioned cue and the outcome is created during extinction, while the original excitatory association stays mostly intact. Also, contextual cues control the expression of this inhibitory association. The more similar the contextual cues at the time of retrieval are to those present during extinction, the more activation of the inhibitory association, producing a higher reduction of responses to the cue. Following these two ideas, extinction and its related phenomena of relapse can be easily explained (Bouton, 2002; Vervliet et al., 2013 for a detailed review).

Bouton et al. (Bouton, Woods, & Pineño, 2004; Woods & Bouton, 2007) found in animal classical and operant conditioning that the rate of reacquisition of a previously extinguished response slowed down when some cue-outcome pairings were included as part of the extinction treatment. Specifically, Bouton et al. (2004) showed, in a series of appetitive classical conditioning experiments, that rats were slower to reacquire a previously extinguished response when the extinction treatment included occasional reinforced trials (i.e., trials in which the cue was followed by an appetitive outcome, food) intermixed among more frequent non-reinforced trials than when extinction only included non-reinforced trials. Woods and Bouton (2007) showed a similar effect in operant conditioning. Rats were slower to reacquire an operant response after an extinction treatment that included intermixed occasional reinforced responses than after a standard extinction treatment including only non-reinforced responses. These results are consistent with the idea that rapid reacquisition may be alleviated in a seemingly paradoxical way namely, intermixing cue alone trials with some trials that also include the outcome.

According to Bouton's model this should occur because in this case reinforced trials, as one of the features present during the acquisition and the extinction phase, become part of both contexts. Later, when the reinforced trials appear during reacquisition, their presence should help activate not only the excitatory context of acquisition but also the inhibitory association formed during extinction, causing a slower reacquisition than in a standard extinction condition where only the acquisition context is retrieved. Consistently with Capaldi's (1967, 1994) sequential learning theory, Ricker and Bouton (1996) suggested that reacquisition is controlled by a "trial-signaling" mechanism, whereby the animal learns that a certain type of trial, either a reinforced or a non-reinforced trial, reliably signals the type of upcoming trial. As a result, during acquisition animals not only learn that the cue is paired by the reinforcer, but also that reinforced trials follow other reinforced trials, whereas during standard extinction animals learnt that non-reinforced trials follow other non-reinforced trials. This way, the type of preceding trial (reinforced or non-reinforced) becomes part of the context that can control responding. Then, including reinforced trials during extinction training, might allow reinforced trials to become associated not only with the acquisition but also with the extinction context. Thus, during reacquisition training, reinforced trials should have also the ability to retrieve the memory of non-reinforced trials (i.e., the inhibitory association learned during extinction training).

These results with non-human animals provide an important starting point, as they show a potential way to reduce relapse and increase the effectiveness of extinction-based treatments. However, no previous evidence of this effect with aversive stimuli has been described in humans to the best of our knowledge.

Thus, the main objective of the present experimental series is to evaluate whether the rate of reacquisition of a previously learned cue-outcome relationship after an extinction treatment varies depending on the inclusion of occasional reinforced trials

during extinction (partial extinction). This evaluation was made with human participants in a contingency learning task including an aversive outcome (see Method for details). From a theoretical point of view, changes in the rate of reacquisition due to this intermixed or partial extinction paradigm would be consistent with Bouton's model predictions concerning the contextual control of the memory stored during extinction. In other words, our objective is to show a potentiated extinction effect as measured by differences in the reacquisition rate after intermixing reinforced trials during extinction and a standard extinction preparation without any reinforced trial. In Experiment 1, the effect of partial extinction was evaluated in a deterministic task (all cue-outcome relationships programmed were deterministic except the for the target partial extinction treatment) whereas in Experiment 2 the effect was evaluated in a probabilistic task (all of the cue-outcome relationships programmed were probabilistic). This way, in Experiment 2, our target evaluation was made in a situation in which both, partial extinction and standard extinction included probabilistic relationships. Experiment 3 tested if a gradual reduction in the probability of reinforcement during extinction could also produce slower reacquisition while having similar levels of responding at the end of the extinction phase.

Experiment 1

Method

Participants and Apparatus

A total of 49 undergraduate Psychology students from University of Málaga completed the task. They received course credits for their participation. Participants conducted the experiment in small groups using a computer room with individual cubicles.

Visual stimuli were presented on a 19-inch monitor with resolution set to 1024 x 768 pixels. Auditory stimuli were presented using individual headphones. The experimental program was written in E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA).

Design and Procedure

The design of the experiment is summarized in Table 1. During Phase 1, both groups of participants were exposed to 18 pairings of cue A with the auditory tone and 18 trials in which cue B was presented alone. The trials were presented in a pseudorandom order. Out of each group of six trials, there were three of each type, with their order randomly selected. This pseudorandom order was used across the whole experiment.

The experimental manipulation took place during Phase 2. Participants in the Intermixed group were exposed to a sequence of 54 trials in which cue A was followed by the outcome on 22.2% of the times. These trials were intermixed with an equal number of trials where cue B was presented alone. To ensure that the transition between Phase 1 and Phase 2, and between Phase 2 and Phase 3 were similar across groups, there was a restriction in the first two and last two trials of cue A, which could not be followed by the outcome. Participants in the Continuous group were exposed to an identical sequence of trials, with the only exception that cue A was never followed by the outcome. In the third and final phase, all participants were exposed to a sequence of 18 trials with cue A always followed by the outcome and 18 trials of cue B presented on its own.

A blue square with size 359×359 pixels and RGB values of 85, 142, 213 and a red circle with diameter 359 pixels and RGB values of 192, 80, 77 were used as cues A and B, counterbalanced across participants. All visual stimuli were presented against a light grey background (RGB values of 128, 128, 128) and centered on the screen. The outcome was a 500 ms white noise at 95 dB (approximately), presented through a set of headphones.

The experiment began with the following instructions, translated from Spanish:

Thank you for participating in this experiment! The task you are about to perform is very simple. During the experiment you will see a series of figures. These figures will sometimes be followed by a noise. Your goal is to predict on each occasion whether or not the noise will be presented. On each trial, you will first see the figure and, below, you will see a rating scale to enter your predictions. To make your prediction, click on any point of the scale. Click on values close to the right extreme (close to the 100 label) if you think that the noise is very likely to follow. If you think that the noise is unlikely to be presented, click on values close to the left extreme (close to zero). When you click on any point of the rating scale, you will see a marker and a label with the specific value you have chosen. If you want to change this value, just click again on a different place of the scale. Once you have chosen the desired value, you can press ENTER to see what happens and check whether the noise is presented or not. Pay attention to the figures and to the noise to learn how to make good predictions. If you have any doubt now or while you are conducting the task, ask the experimenter for help and make sure that you understand everything. Good luck!

Each trial began with a black fixation cross (Courier New font, size 180) presented on the center of the screen for 2500 to 3500 ms (uniform distribution with 100 ms step). Afterwards, the cue was presented together with a rating scale on the lower part of the screen where participants had to click to enter their response following the procedure described in the instructions. The cue remained on screen for 3000 ms after participants had responded. The outcome, when present, overlapped with the time period of 2000 to 2500 ms after the onset of the cue. At the end of the trial, all visual and auditory stimuli were removed and the fixation cross of the next trial was presented.

Results and Discussion

Pre-analysis treatment of data

Before the analysis, we removed the data from those participants whose mean score of the three last trials of Phase 1 for either cue A or cue B was more than 2 standard deviations away from the group mean (filters 1 and 2). The same selection criterion was applied to the three last trials of cue B in Phase 2 (filter 3). These filters were chosen because they ensured an adequate level of similar performance between participants in situations non-related to the effect of interest (filter 3) and previous to the experimental manipulation (filters 1 and 2). Four participants did not meet the filter criteria described and were removed from further analyses. The final sample consisted of 45 participants (20 in the Intermixed group, 25 in the Continuous group).

Statistical analyses

All the statistical analyses were performed using IBM SPSS version 21 (IBM Corp., 2012). In all the repeated measures ANOVAs the sphericity was tested and the degrees of freedom were corrected using Greenhouse-Geisser's epsilon whenever necessary. The curve fitting procedures were carried out using Matlab version 2012b and its Curve Fitting Toolbox (The MathWorks, Inc., 2012). The effect size statistics reported are partial eta squared (η^2_p) for the ANOVAs and Cohen's d in the case of the t tests (Cohen, 1988).

Acquisition Phase

The top panel of Figure 1 depicts the results for the Acquisition phase. A mixed ANOVA was used to analyze these data, which included a between-subjects factor (Group: Intermixed vs. Continuous) and two within-subjects factors (Cue: A vs. B, and Trial: 1 to

18). The results showed a significant effect of Cue, Trial and Cue \times Trial interaction (respectively [$F(1, 43) = 2314.37, p < .001, \eta^2_p = .981$], [$F(6.74, 289.98) = 2.41, p = .022, \eta^2_p = .053$] and [$F(5.23, 224.98) = 43.76, p < .001, \eta^2_p = .504$]). We observed no significant effect of the Group factor during acquisition, as there was no main effect of Group [$F(1, 43) = 0.6, p = .442, \eta^2_p = .014$], nor Group \times Cue [$F(1, 43) = 0.3, p = .582, \eta^2_p = .007$], Group \times Trial [$F(6.74, 289.98) = 1.83, p = .083, \eta^2_p = .04$] or Group \times Cue \times Trial interactions [$F(5.23, 224.98) = 0.41, p = .847, \eta^2_p = .009$].

Extinction Phase

A similar ANOVA was performed with the data of the Extinction phase, shown in the middle panel of Figure 1. It showed a significant effect of Group [$F(1, 43) = 39.88, p < .001, \eta^2_p = .481$], Cue [$F(1, 43) = 96.19, p < .001, \eta^2_p = .691$], Trial [$F(11.27, 484.98) = 20.55, p < .001, \eta^2_p = .323$], Group \times Cue [$F(1, 43) = 33.13, p < .001, \eta^2_p = .435$], Cue \times Trial [$F(9.94, 427.69) = 9.32, p < .001, \eta^2_p = .178$] and Group \times Cue \times Trial interactions [$F(9.94, 427.69) = 2.52, p = .005, \eta^2_p = .055$]. The Group \times Trial contrast was not significant [$F(11.27, 484.98) = 1.57, p = .101, \eta^2_p = .035$]. As can be seen in Figure 1, this was due to the fact that responses to cue A differed between Intermixed and Continuous groups, with that difference varying across trials. This was confirmed with an additional ANOVA with two factors, Group (Intermixed vs. Continuous) and Trial (1 to 18) of the responses to cue A. There was a main significant effect of the two factors (Group, [$F(1, 49) = 27.9, p < .001, \eta^2_p = .363$], Trial, [$F(11.86, 581.38) = 16.26, p < .001, \eta^2_p = .249$]) and a significant interaction between them (Group \times Trial, [$F(11.86, 581.38) = 2.36, p = .006, \eta^2_p = .046$]). In the case of the responses to cue B, there was no significant effect of Group, Trial, or Group \times Trial interaction ($F_s < 1.37, p_s > .247$).

Reacquisition Phase

Data from the Reacquisition phase are shown in the bottom panel of Figure 1. A three-way ANOVA was used using the same factors as in the case of the Acquisition phase analysis. There was no main effect of Group [$F(1, 43) = 3.07, p = .087, \eta^2_p = .067$], but there were significant effects of Cue [$F(1, 43) = 974.71, p < .001, \eta^2_p = .957$] and Trial factors [$F(5.77, 248.5) = 39.97, p < .001, \eta^2_p = .481$], and significant Group \times Trial [$F(5.77, 248.5) = 7.01, p < .001, \eta^2_p = .14$], Cue \times Trial [$F(6, 258.17) = 58.98, p < .001, \eta^2_p = .578$], and Group \times Cue \times Trial interactions [$F(6, 258.17) = 6.15, p < .001, \eta^2_p = .125$]. The Group \times Cue [$F(1, 43) = 2.54, p = .118, \eta^2_p = .055$] interaction was not significant.

Given the results observed and our previous hypothesis, we tested the possibility that the reacquisition of cue A could have differed between groups. To do so, we analyzed only responses to cue A in both groups, using an ANOVA with only the Group and Trial factors. It showed that there was no main effect of Group [$F(1, 43) = 2.86, p = .098, \eta^2_p = .062$] but there was a main effect of Trial [$F(5.35, 229.88) = 60.83, p < .001, \eta^2_p = .586$]. Crucially for our hypothesis, there was a significant interaction between these two factors, Group \times Trial [$F(5.34, 229.87) = 8.09, p < .001, \eta^2_p = .158$]. As expected, this pattern of results did not happen in an equivalent analysis for cue B, where there were no significant effects of Group nor a Group \times Trial interaction ($F_s < 1.27, p_s > .283$).

Post hoc *t*-tests for independent samples were run on the responses to cue A on each trial, finding statistical differences between groups in Trial 1 [$t(28.25) = 3.99, p < .001, d_s = 1.27$], Trial 2 [$t(43) = 3.06, p = .004, d_s = 0.92$], Trial 3 [$t(43) = 3.64, p = .001, d_s = 1.09$] and Trial 4 [$t(43) = 2.75, p = .009, d_s = 0.765$].

Curve Fitting

Given the negatively accelerated shape of the reacquisition learning curve, it is also possible to carry out a model fitting analysis. We can try to estimate a curve that describes the behavior of each group as a function of the number of trials elapsed. As 100 was the maximum value of participants' responses, a very simple curve equation would be the following one:

$$\text{Equation 1: } y = 100 - \left(\frac{100}{a + x^b} \right)$$

In this equation, y would be the response observed to cue A and x the number of the current trial. There are two free parameters a and b representing respectively the initial level of responding right before the beginning of the reacquisition phase and the slope or acceleration of the curve. As the value of b increases, the curve takes fewer trials to reach its asymptote, while with lower values it takes a greater number to reach it. We estimated for each group the values of a and b (see Figure 2). This estimation was done considering all data points for each trial and used the Curve Fitting toolbox of Matlab, and its implementation of the Trust Region non-linear least squares algorithm (Branch, Coleman, & Li, 1999). In the Intermixed group, parameters a and b that produced the best fitting results were 0.363 (95% C.I., 0.184, 0.541) and 0.759 (95% C.I., 0.68, 0.838), respectively, $R^2 = .332$. In the Continuous group, best-fitting a and b parameter values were 0.061 (95% C.I., -0.036, 0.159) and 1.409 (95% C.I., 1.243, 1.576), respectively, $R^2 = .453$. This indicated that there was a statistically significant difference between the acceleration parameters of the reacquisition curves in both groups, as parameter b values differed across groups.

Experiment 2

The results of Experiment 1 suggest that, in comparison to a standard extinction procedure, a probabilistic extinction might be effective at slowing down the rate of reacquisition. However, in Experiment 1 only participants in the Intermixed group were exposed to a probabilistic cue-outcome relation at some point of the experiment. That is, only in this group one of the cues (cue A) was not a perfect predictor of the presence or absence of the outcome (specifically, in Phase 2 it predicted the absence of the outcome in 77.8% of the cases and its presence in the other 22.2% of the cases) whereas in the other group all cues within each of the phases had a deterministic, perfect relationship with the outcome. It is possible that the slower learning rate observed at test is not due to the fact that the target cue was extinguished following a partial reinforcement procedure, but to the simple fact that participants in the Intermixed group were exposed to a probabilistic contingency that increased uncertainty about the task in general and reduced participants' confidence about the consistency of cue-outcome relations. In Experiment 2 all participants were exposed to probabilistic cue-outcome relations during the three phases of the experiments and thus, we tried to generalize the differential reacquisition results obtained to a situation in which uncertainty is increased and not limited to the target partial extinction phase. As can be seen in the design summary shown in Table 2, this was achieved by including a third cue in both groups that was partially reinforced during the whole sequence of trials, as well as making the acquisition of cue A also probabilistic.

Method

Participants and Apparatus

Sixty-nine undergraduate Psychology students from University of Málaga participated in the experiment and received course credits for it. All of them were tested under the same conditions as in Experiment 1.

Design and Procedure

Unless stated otherwise, all procedural details and design were as in Experiment 1. The main difference with respect to the previous experiment was the inclusion of a third cue, C, that held a probabilistic relation with the outcome throughout all phases of the experiment. The additional cue employed was a yellow triangle (RGB 255, 242, 0) of height and base of 359 pixels. As in Experiment 1, the role of each of the stimuli was counterbalanced across participants.

The number of trials of each type was also reduced at variance with Experiment 1 to compensate for the extra cue included. As shown in Table 2, during Phase 1 all participants were exposed to 8 trials in which the outcome followed cue A in 7 of those trials (87.5% of the trials were reinforced). Participants were also exposed to 8 trials of cue B presented without the outcome, and 8 trials in which cue C was followed by the outcome 12.5% of the times (1 out of 8 trials). As in Experiment 1, trials were presented in a pseudorandom order. The experimental manipulation took place during Phase 2, where participants in the Intermixed group were exposed to 24 trials of cue A followed by the outcome 12.5% of the time, while for participants in the Continuous group cue A was never followed by the outcome. In both groups, these trials were intermixed with 24 trials with cue B presented on its own and 24 trials with cue C followed by the outcome as in Phase 1, 12.5% of the times. During the third and final phase, all participants were exposed to 10 trials with cue A followed by the outcome, 10 trials with B alone, and 10 trials with the probabilistic cue C followed by the outcome 10% of the times.

Results and Discussion

Pre-analysis treatment of data

Ten participants (4 from the Intermixed group and 6 from the Continuous group) did not meet the inclusion criteria described in Experiment 1 and were excluded from further analyses. After this, the Intermixed group had 30 participants, while the Continuous group had 29 participants.

Statistical Analyses

All the statistical analyses were the same as in Experiment 1, with the only exception of the number of trials, and the Cue factor, that in this experiment had three levels as it included also cue C. As in the previous experiment, whenever the sphericity assumption was violated, the Greenhouse-Geisser correction was applied.

Acquisition Phase

The top panel of Figure 3 depicts the results for the Acquisition phase. The Group \times Cue \times Trial mixed ANOVA showed main effects of Cue [$F(1.78, 101.24) = 567.68, p < .001, \eta^2_p = .909$] and Trial [$F(4.97, 283.42) = 2.41, p = .037, \eta^2_p = .041$], but not of Group [$F(1, 57) = 0.08, p = .775, \eta^2_p = .001$]. The interactions between Group \times Cue [$F(1.78, 101.24) = 0.95, p = .38, \eta^2_p = .016$] and Group \times Trial [$F(4.97, 283.42) = 0.4, p = .848, \eta^2_p = .007$] were not significant. As expected, the Cue \times Trial interaction [$F(7.82, 445.55) = 20.77, p < .001, \eta^2_p = .267$] was statistically significant. This interaction together with the Cue main effect indicated that the different contingencies programmed for each cue lead to different levels of responding, and that the differences between them were acquired across

time. There was no Group \times Cue \times Trial interaction [$F(7.82, 445.55) = 0.39, p = .922, \eta_p^2 = .007$]. Given that none of the contrasts including the Group factor were significant, we can conclude that there were no differences between groups during acquisition.

Extinction Phase

The results for the Extinction Phase are shown in the middle panel of Figure 3. During extinction, we found significant main effects of Group [$F(1, 57) = 9.71, p = .003, \eta_p^2 = .145$], Cue [$F(1.58, 90.3) = 81.1, p < .001, \eta_p^2 = .587$] and Trial [$F(10.95, 624.42) = 20.18, p < .001, \eta_p^2 = .261$], as well as Group \times Cue [$F(1.58, 90.3) = 21.77, p < .001, \eta_p^2 = .276$] and Cue \times Trial interactions [$F(16.35, 932.04) = 13.13, p < .001, \eta_p^2 = .187$]. The Group \times Trial [$F(10.95, 624.42) = 1.58, p = .101, \eta_p^2 = .027$] and Group \times Cue \times Trial interactions [$F(16.35, 932.04) = 0.93, p = .534, \eta_p^2 = .016$] were not statistically significant. As in the case of Experiment 1, these results were due to the differences observed in cue A. When the ANOVA analyses were repeated separating across cues, there was a significant effect of Group and a Trial \times Group interaction (respectively [$F(1, 57) = 27.39, p < .001, \eta_p^2 = .325$] and [$F(11.42, 651.11) = 1.92, p = .033, \eta_p^2 = .033$]) for cue A, but not for cues B or C (all F s < 1).

Reacquisition Phase

The bottom panel of Figure 3 depicts the results of the Reacquisition Phase. As in Experiment 1, the data obtained in the Reacquisition phase showed no main effect of Group [$F(1, 57) = 1.63, p = .206, \eta_p^2 = .028$] or Group \times Cue interaction [$F(1.52, 86.77) = 1.37, p = .257, \eta_p^2 = .023$], but there was a significant Group \times Cue \times Trial interaction [$F(9.59, 546.4) = 2.27, p = .014, \eta_p^2 = .038$]. Additionally, there were significant effects of Cue [$F(1.52, 86.77) = 374.14, p < .001, \eta_p^2 = .868$], Trial [$F(5.74, 327.18) = 34.7, p < .001,$

$\eta^2_p = .378$], Group \times Trial [$F(5.74, 327.18) = 5.04, p < .001, \eta^2_p = .081$] and Cue \times Trial interactions [$F(9.59, 546.4) = 42.3, p < .001, \eta^2_p = .426$].

In order to follow up the critical Group \times Cue \times Trial interaction, we ran separate analysis for each of the cues. In the case of cue A we found a marginally significant Group effect [$F(1, 57) = 3.31, p = .074, \eta^2_p = .055$] and significant effects of Trial [$F(5.02, 286.33) = 81.29, p < .001, \eta^2_p = .588$] and a Group \times Trial interaction [$F(5.02, 286.33) = 5.47, p < .001, \eta^2_p = .088$]. This indicated that the differences between the two groups varied significantly across trials. The main effect of Group and the Group \times Trial interaction were non-significant for cues B ($F_s < 1.26, p_s > .28$) and C ($F_s < 1.15, p_s > .33$).

A series of post-hoc t tests were run for differences between responses to cue A from both groups across the different trials, showing that there were significant differences in Trial 1 [$t(35.16) = 3.64, p < .001, d_s = 0.681$], Trial 4 [$t(57) = 2.25, p = .028, d_s = 0.479$], Trial 7 [$t(42.03) = 3.66, p < .001, d_s = 0.704$], Trial 9 [$t(43.79) = 2.77, p = .008, d_s = 0.537$] and Trial 10 [$t(43.44) = 2.54, p = .015, d_s = 0.49$]. As can be seen in Figure 3, differences found in Trial 1 and those in the rest of trials were of opposite directions. Whereas mean responses for the Intermixed group were higher in Trial 1, they were significantly lower in the rest of the trials.

Curve Fitting

The same procedure described for Experiment 1 was applied also to the data from Experiment 2. The best-fitting curves are shown in Figure 4. The parameters a and b that produced best-fitting results for the Intermixed group were $a = 0.291$ (C.I. 95%, 0.142, 0.439) and $b = 0.668$ (C.I. 95% 0.586, 0.751), respectively, $R^2 = .32$ for the model. In the case of the Continuous group their values were $a = 0.003$ (C.I. 95% -0.08 to 0.085) and b

= 0.996 (C.I. 95% of 0.903 to 1.09), being the variance that the model explained $R^2 = .596$.

As in Experiment 1, the value of parameter b was significantly higher in the Continuous than in the Intermixed Group, indicating that reacquisition was faster in the former than in the latter group.

Experiment 3

The consistent pattern of results observed in Experiments 1 and 2 provides strong support for the hypothesis that a probabilistic extinction slows down the rate of reacquisition. However, this conclusion is potentially undermined by a common problem of both experiments. In both cases, the experimental manipulation not only affected the rate of reacquisition, but also the asymptotic level of performance during extinction. By the end of extinction, participants in the Intermixed group were still showing a substantial amount of responding to the extinguished cue A. Perhaps it is the incomplete extinction of A, and not the probabilistic extinction per se, that explains why reacquisition was slower in the Intermixed group.

In Experiment 3 we implemented an additional change in the design to achieve complete extinction of A by the end of the extinction stage. Specifically, the proportion of reinforced cue A trials was reduced progressively during the initial blocks of extinction so that, by the end of that stage, only non-reinforced cue A trials were presented. As can be seen in the design summary shown in Table 3, the last blocks of extinction included only non-reinforced trials in both groups. Because of this, we expected that their levels of responding would eventually converge to similar values. However, the predictions derived from Bouton's model are not affected by these changes: Even if all participants reach similar levels of responding during extinction, those in the Intermixed group should still show slower learning during reacquisition as reinforced trials were still part of the

extinction context, that is, they still experienced reinforced trials followed by non-reinforced trials.

Method

Participants and Apparatus

Seventy undergraduate Psychology students from University of Málaga participated in the experiment and received course credits for it. All of them were tested under the same conditions as in Experiments 1 and 2.

Design and Procedure

The design of the experiment was largely based on Experiment 2, except for two crucial differences. Firstly, to shorten the experiment as much as possible, the probabilistic cue C was not included in Experiment 3. As in Experiment 1, only two cues were used throughout the sequence of trials. The assignment of stimuli to cues was counterbalanced across participants. Secondly, in order to obtain complete extinction we included a longer sequence of extinction trials. Therefore, participants were exposed to 56 cue A trials and 56 non-reinforced cue B trials during Phase 2. In the Intermixed group, the percentage of reinforced trials of cue A decreased progressively, with 5 of the first 8 trials being reinforced, 3 of the second 8 trials, 1 of the third 8 trials, and none of the last 32 trials. In the Continuous group, all 56 cue A trials were non-reinforced. Apart from these two modifications, the design and procedure were as in Experiment 2.

Results and Discussion

Pre-analysis treatment of data

Given that the objective of the experiment was to test the effect of intermixed extinction after reaching an asymptotic level of extinction, we added an additional exclusion criterion, similar to those used in Experiments 1 and 2. Data from participants whose mean responses for cue A in the last three trials of extinction was more than 2 standard deviations away from the overall group mean were excluded from further analyses. Six participants from the Continuous group did not meet the inclusion criteria described in Experiment 1 or the additional criterion just mentioned. After this, the Intermixed group included 35 participants, while the Continuous group included 29 participants.

Statistical Analyses

All the statistical analyses were the same as in Experiment 1, with the only exception of the number of trials in the acquisition and reacquisition stages. As in previous experiments, the Greenhouse-Geisser correction was applied when necessary.

Acquisition Phase

The top panel of Figure 5 depicts the results for the Acquisition phase. The Group \times Cue \times Trial mixed ANOVA showed main effects of Cue [$F(1, 63) = 2829.35, p < .001, \eta^2_p = .979$] and Trial [$F(1.87, 115.76) = 8.45, p < .001, \eta^2_p = .12$]. As expected, the Cue \times Trial interaction was statistically significant [$F(2.88, 178.47) = 131.48, p < .001, \eta^2_p = .679$]. All

other effects and interactions were non-significant [largest $F = 1.34$, smallest $p = .251$].

These results show that both groups learned equally the target cue-outcome contingencies.

Extinction Phase

The middle panel of Figure 5 shows the results for the Extinction Phase. The Group \times Cue \times Trial ANOVA on predictive judgments yielded main effects of Cue [$F(1, 62) = 219.74, p < .001, \eta^2_p = .78$], Trial [$F(14.19, 879.49) = 76.41, p < .001, \eta^2_p = .552$] and Group [$F(1, 62) = 91.82, p < 0.001, \eta^2_p = 0.597$]. The Group \times Cue [$F(1, 63) = 100.82, p < .001, \eta^2_p = .619$], Group \times Trial [$F(14.185, 879.49) = 27.63, p < .001, \eta^2_p = .308$], and Cue \times Trial [$F(13.12, 813.44) = 57.73, p < .001, \eta^2_p = .48$] interactions were all statistically significant. Furthermore, the double Group \times Cue \times Trial interaction was also significant [$F(13.12, 813.44) = 24.47, p < .001, \eta^2_p = .283$].

An additional analysis of cue A showed significant effects of Trials [$F(13.35, 827.81) = 73.78, p < 0.001, \eta^2_p = 0.543$] and the Trials \times Group interaction [$F(13.35, 827.81) = 28.65, p < 0.001, \eta^2_p = 0.316$]. As can be seen, this interaction is due to the different course of extinction of cue A in each group. However, a series of t -tests confirmed that there were no significant differences across groups in responding to cue A in the last 8 trials (all $ps > .157$, with all the differences between means of the groups under 3.38 points), indicating that the same level of extinction had been reached in both groups at the end of the extinction phase, at variance with the results from previous experiments.

Reacquisition Phase

The bottom panel of Figure 5 depicts the results of the Reacquisition Phase. As in Experiments 1 and 2, the main effect of Group [$F(1, 62) = 2.219, p = .141, \eta^2_p = .035$], and the Group \times Cue interaction [$F(1, 62) = 1.81, p = .183, \eta^2_p = .028$] failed to reach statistical

significance. However, we found significant effects of Cue [$F(1, 62) = 2399.17, p < .001, \eta^2_p = .975$], Trial [$F(3.11, 192.68) = 263.44, p < .001, \eta^2_p = .809$], Group \times Trial [$F(3.11, 192.68) = 5.60, p < .001, \eta^2_p = .083$], and Cue \times Trial interactions [$F(3.87, 239.91) = 198.59, p < .001, \eta^2_p = .762$]. Most importantly, we also found a significant Group \times Cue \times Trial interaction [$F(3.87, 239.91) = 5.32, p < .001, \eta^2_p = .079$].

To further explore the critical Group \times Cue \times Trial interaction, we ran separate analysis for each of the cues. Judgments for cue A showed a significant effect of Trial [$F(2.77, 171.55) = 278.97, p < .001, \eta^2_p = .818$] and a significant Group \times Trial interaction [$F(2.77, 171.55) = 6.46, p < .001, \eta^2_p = .094$]. This interaction confirms that the rate of reacquisition of cue A differed between groups. The main effect of Group did not reach statistical significance [$F(1, 62) = 2.07, p = .155, \eta^2_p = .032$]. In the case of judgments for cue B, none of the main effects or the interaction was statistically significant (all $ps > 0.394$).

A series of post-hoc t tests were run for differences between responses to cue A from both groups across the different trials, showing that there were significant differences in Trial 2 [$t(59.05) = 3.12, p = .003, d_s = 0.783$] and Trial 3 [$t(61.73) = 2.06, p = .044, d_s = 0.517$]. Judgments for A did not differ significantly in the rest of the trials [largest $t = 1.13$, smallest $p = .265$].

Curve Fitting

We computed the best-fitting curves to the reacquisition of cue A following the procedure described in previous experiments. Figure 6 depicts the best-fitting curves. The parameters a and b that produce best-fitting results for the Intermixed group were $a = -0.020$ (C.I. 95%, -0.079, 0.039) and $b = 1.268$ (C.I. 95% 1.167, 1.369), respectively, $R^2 = .72$ for the model. In the case of the Continuous group their values were $a = 0.040$ (C.I.

95% -0.037 to 0.117) and $b = 1.718$ (C.I. 95% of 1.508 to 1.929), being the variance that the model explained $R^2 = .66$. As in Experiments 1 and 2, the best-fitting parameter b was significantly higher in the Continuous than in the Intermixed Group, confirming that reacquisition was faster in the former group.

General Discussion

The results reported provide evidence of a slower reacquisition after an intermixed or partial extinction procedure in human contingency learning. Specifically, the rate or reacquisition of a previously extinguished response was lower after a partial than after a standard extinction procedure. This effect appeared when control conditions consisted of deterministic cue-outcome relationships (Experiment 1) as well as probabilistic cue-outcome relationships (Experiment 2). And importantly, Experiment 3 showed that the differential reacquisition was still obtained even when expectancy judgments had reached asymptotic levels of extinction. Thus, slower reacquisition cannot be regarded as a by-product of a previous incomplete extinction but the genuine effect of intermixing reinforced trials during the extinction treatment.

In Experiments 1 and 2, responses to cue A differed in both groups of participants at the end of the extinction phase. This happened even when the probability of reinforcement was relatively low (12.5% in Experiment 2). This fact introduces a potential confound in the interpretation of the results, as it makes it harder to compare the reacquisition rate of both groups. However, we would argue that in fact this supports the robustness of the effect. Although participants in the Continuous group had lower levels of responding at the end of the extinction phase than those in the Intermixed Group, participants' responses from the former group increased during the initial trials of the reacquisition phase. Therefore, should both groups had reached the same level of responding at the end of the

extinction phase, even sharper differences between groups would be expected during the first reacquisition trials. This conclusion is supported by our curve fitting results.

Parameter b , which represented the reacquisition rate, was lower in the Intermixed groups even when controlling for the initial level of responding during the reacquisition phase (Parameter a). On the other hand, the results from Experiment 3 proved that the slower reacquisition effect was not due to differences in the response level at the end of the extinction phase in both groups, but to the partial extinction programmed.

The high level of responding obtained despite the low number of reinforced trials in Experiments 1 and 2 may have been due to changes in the level of unconditioned responding to the outcome. It has been suggested that the level of unconditioned responding produced by an aversive stimulus can vary due to several factors. Repeated presentation of the outcome can lead to its habituation (e.g., Rescorla, 1973), and whenever an outcome is correctly anticipated, the level of unconditioned responding is reduced (Dunsmoor, Bandetinni, & Knight, 2008; Grings, 1973; Lykken & Tellegen, 1974), and made less aversive (Schell & Grings, 1971). In our experiments, a reduction in the predictability of the outcome could have led to an increase in its aversiveness, causing higher levels of conditioned responding. Consistently with this idea, response levels in Experiment 3 extinguished completely when the reinforcement schedule diminished progressively during extinction, rendering the absence of the outcome more and more predictable

Overall, the pattern of results obtained mimicked the target effect found in the animal conditioning literature (Bouton et al., 2004; Gershman, Jones, Norman, Monfils, & Niv, 2013; Woods & Bouton, 2007). To the best of our knowledge, there is only another demonstration of a similar partial extinction manipulation in human learning. van den Akker, Havermans, and Jansen (2015) have showed a slowed reacquisition of verbal

expectancy, using food as an outcome in an appetitive task. Put together, these findings point to the possibility of a general effect across types of reinforcers, although more evidence is required.

Although the level of uncertainty (i.e., non-deterministic cue-outcome relationships) in Experiments 2 and 3 was more similar across groups than in Experiment 1, they were not completely equated. Previous studies have shown that increased uncertainty can lead to higher learning rates (e.g., Behrens, Woolrich, Walton, & Rushworth, 2007; Courville, Daw, & Touretzky, 2006; although see Le Pelley, 2004 and Le Pelly & McLaren, 2003). However, our results show the opposite pattern of results, as the Intermixed group, in which the level of uncertainty during extinction was higher than in the Continuous group, showed a slower learning rate during the reacquisition phase. Therefore, it is hard to explain the pattern of data obtained solely on this difference of uncertainty between the conditions.

On the other hand, our results are compatible with the theoretical proposal by Bouton et al. (2004). According to this account, when extinction takes place, reinforced trials become a cue that indicates whether the current context is the extinction or the acquisition context. This potential role of the reinforced trials as a contextual cue is degraded by introducing these reinforced trials during the extinction phase. Thus, reinforced trials would not univocally signal the acquisition context, which in turn, would finally lead to a slower reacquisition. But this is not the only explanation available, as other theoretical models for this effect have been put forward. For example, according to Gershman, Blei, and Niv (2010) the mechanism involved would be quite different. They propose that persisting large prediction error provide a signal that is used to segment learning. Future trials will be coded as part of a new context, with new associations. In the case of Experiment 3 according to this theory, persisting large prediction errors would occur

during the change from the acquisition to the extinction phase in the case of our control groups. This would be due to the sudden shift from a reinforced to a non-reinforced scenario. However, this should take place to a lesser extent in the case of the experimental group, which changes from a reinforced to a partially reinforced scenario. In the former, acquisition and extinction would be encoded in separate associations, as they would be segmented in different contexts, while in the latter a single association would be updated across the trials of both phases (see Gershman et al., 2013 for a detailed discussion).

The main objective of this study was to provide evidence of the effect of partial reinforcement during extinction in human contingency learning, and more experiments are required to better understand the mechanisms underlying this effect. For example, in our curve fitting analysis, we have implicitly assumed that reacquisition can be modeled as a negatively accelerated curve with different learning rates in each group. However, this might not be necessarily the case. Authors like Charles R. Gallistel (Gallistel 2012a, 2012b; Gallistel, Fairhurst, & Balsam, 2004) have proposed that learning is better described as an all-or-nothing process, in which organisms switch between multiple states that have different levels of response. From this point of view, the learning curve described in most studies is only the effect of averaging the responses of multiple participants who make this transition at different moments. This could have happened in this series of experiments. Specific data analyses, beyond the scope of this work, have to be used to properly test this possibility and differentiate between these two proposals (see Blanco & Morís, 2016, for an extended discussion of this problem and possible data analysis solutions based on Bayesian modelling). Also, it must be noted that theories like Bouton's model can easily accommodate both types of mechanism. Additionally, the implications of both potential mechanisms for relapse reduction are not substantially different either. No matter whether the partial extinction treatment has altered the learning rate of reacquisition

or has delayed the moment when participants detect the new contingency, relapse may be understood as having been reduced. Future experiments are needed to specifically test what mechanisms underlie this phenomenon in humans, their boundary conditions and how to optimize the reduction of relapse.

The relevance of the results from Experiment 3 is not only theoretical. The pattern of results obtained in Experiment 3 showed that partial extinction may potentiate extinction effects even if maximal extinction has already been achieved. Of course, reaching the lowest possible levels of responding once extinction is complete constitutes one of the most important therapeutic outcomes in anxiety disorder treatments. The results of Experiment 3 showed that a partial extinction procedure does not prevent complete extinction of expectancy ratings. Although these results are still far from being directly applicable to clinical scenarios, they suggest that partial extinction is not necessarily an obstacle to reach low levels of conditioned responding.

In order to explore more thoroughly the possible clinical implications of the effect found, it would be necessary to know whether similar effects may be obtained using a more aversive paradigm (note the mild aversive sound used in our task) and registering alternative responses to expectancy ratings, such as subjective fear ratings or behavioral responses e.g., the potentiated startle response or avoidance behavior, that might also reflect more emotional aspects of fear. These different measures may too be tapping different processes engaged in human learning that may interact in different ways and, importantly, that can be dissociated (e.g., Morís, Cobos, Luque, & López, 2014; Sevenster, Beckers, & Kindt, 2012; Soeter & Kindt, 2011). However, this interest should not obscure the relevance of expectancy ratings themselves, as danger expectancies play an important role in cognitive theories of fear and anxiety and these expectancy ratings may be regarded

as a highly valid measure of fear conditioning (see Boddez, Bayens, Luyten, Vansteenwegen, Hermans, & Beckers, 2013).

Slower reacquisition can be of great applied relevance in those situations in which the patient might have to experience again the aversive situation leading to the emotional disorder, either due to observational learning (Askew & Field, 2008; Todd & Pietrowski, 2007), or a direct reexposure, like in the case of social phobias or post-traumatic stress disorder (Craske et al., 2014). For example, patients suffering from social anxiety disorder may re-experience, after exposure therapy, a truly aversive event related to social failure (e.g., a deeply embarrassing or traumatic situation in a social context), that may be viewed as a reacquisition experience. Our result suggests the idea that a partial version of exposure therapy may induce some form of resilience to manage future re-encounters with truly anxiogenic social situations. Nonetheless, this is not the most widespread relapse effect, nor the most common experimental model of relapse. Finding an equivalent alleviating effect of these other forms of relapse may, in principle, increase the clinical interest of the results found. Only future research will have a say in this.

Due to its easy implementation, and its potential use to reduce relapse, intermixed extinction might constitute in the future a way to improve extinction-based therapies. It is also a very interesting phenomenon to further develop the theories of associative learning and extinction, and it can serve as an experimental tool to further test their predictions. Moreover, there are many open questions regarding this effect, its boundary conditions, and how to maximize it. All in all, it may be regarded as a promising venue of research.

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Table 1

Design summary of Experiment 1. The percentage of trials in which cues A and B were paired with the outcome is indicated between brackets

Group	Phase 1	Phase 2	Phase 3
Intermixed	18 x A (100%)	54 x A (22.2%)	18 x A (100%)
	18 x B (0%)	54 x B (0%)	18 x B (0%)
Continuous	18 x A (100%)	54 x A (0%)	18 x A (100%)
	18 x B (0%)	54 x B (0%)	18 x B (0%)

Table 2

Design summary of Experiment 2. The percentage of trials in which cues A, B and C were paired with the outcome is indicated between brackets

Group	Phase 1	Phase 2	Phase 3
Intermixed	8 x A (87.5%)	24 x A (12.5%)	10 x A (100%)
	8 x B (0%)	24 x B (0%)	10 x B (0%)
	8 x C (12.5%)	24 x C (12.5%)	10 x C (10%)
Continuous	8 x A (87.5%)	24 x A (0%)	10 x A (100%)
	8 x B (0%)	24 x B (0%)	10 x B (0%)
	8 x C (12.5%)	24 x C (12.5%)	10 x C (10%)

Table 3

Design summary of Experiment 3. The percentage of trials in which cues A and B were paired with the outcome is indicated between brackets. During Phase 2 in the Intermixed group, the percentage of reinforced trials of cue A decreased progressively, with 5 of the first 8 trials being reinforced, 3 of the second 8 trials, 1 of the third 8 trials, and none of the last 32 trials.

Group	Phase 1	Phase 2	Phase 3
Intermixed	8 x A (87.5%)	56 x A (16%)	10 x A (100%)
	8 x B (0%)	56 x B (0%)	10 x B (0%)
Continuous	8 x A (87.5%)	56 x A (0%)	10 x A (100%)
	8 x B (0%)	56 x B (0%)	10 x B (0%)

Figure Captions

Figure 1. Mean predictive judgements of each of the three phases in Experiment 1.

Acquisition, Extinction and Reacquisition are presented in the top, middle and bottom panels, respectively. The error bars are the standard error of the mean.

Figure 2. Data points of all the participants from each group (Intermixed group, blue dots and blue line, Continuous group, red dots and red line) in Experiment 1, representing predictive judgements for each trial. The line depicted is the non-linear function that was fitted to these data. Each data point has been displaced a small random distance in the horizontal axis to facilitate its visual display.

Figure 3. Mean predictive judgements of each of the three phases in Experiment 2.

Acquisition, Extinction and Reacquisition are presented in the top, middle and bottom panels, respectively. The error bars are the standard error of the mean.

Figure 4. Data points of all the participants from each group (Intermixed group, blue dots and blue line, Continuous group, red dots and red line) in Experiment 2, representing predictive judgements for each trial. The line depicted is the non-linear function that was fitted to these data. Each data point has been displaced a small random distance in the horizontal axis to facilitate its visual display.

Figure 5. Mean predictive judgements of each of the three phases in Experiment 3.

Acquisition, Extinction and Reacquisition are presented in the top, middle and bottom panels, respectively. The error bars are the standard error of the mean.

Figure 6. Data points of all the participants from each group (Intermixed group, blue dots and blue line, Continuous group, red dots and red line) in Experiment 3, representing predictive judgements for each trial. The line depicted is the non-linear function that was fitted to these data. Each data point has been displaced a small random distance in the horizontal axis to facilitate its visual display.

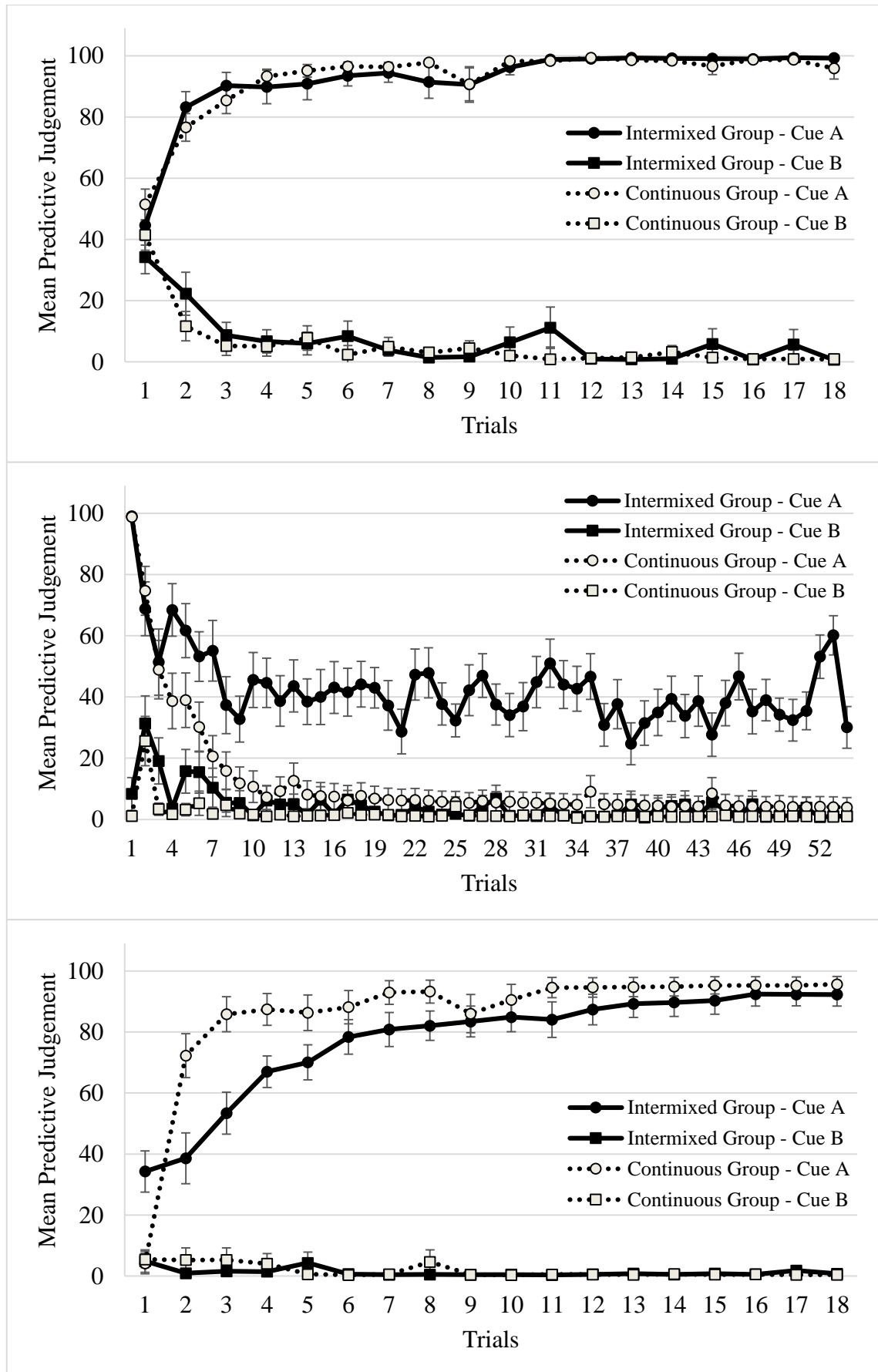


Figure #1

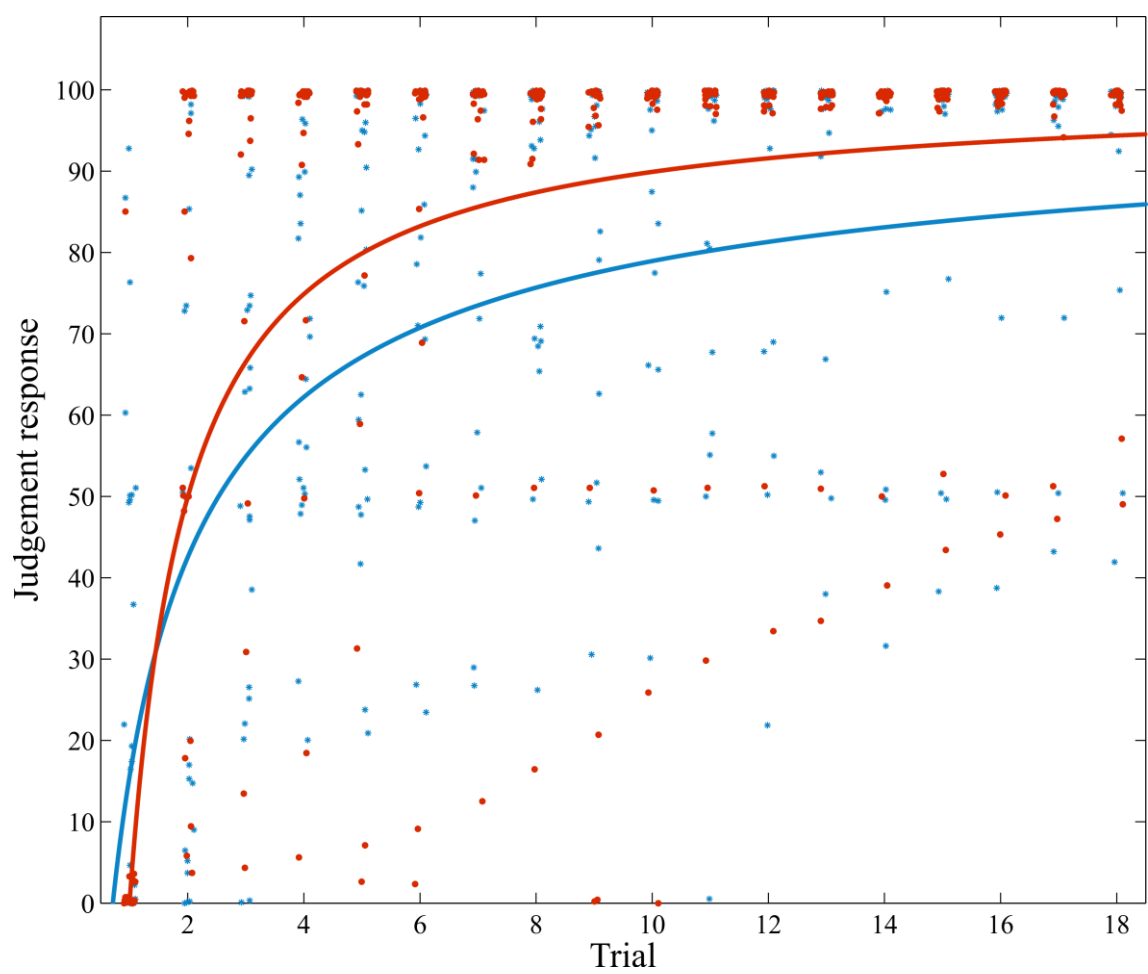


Figure #2

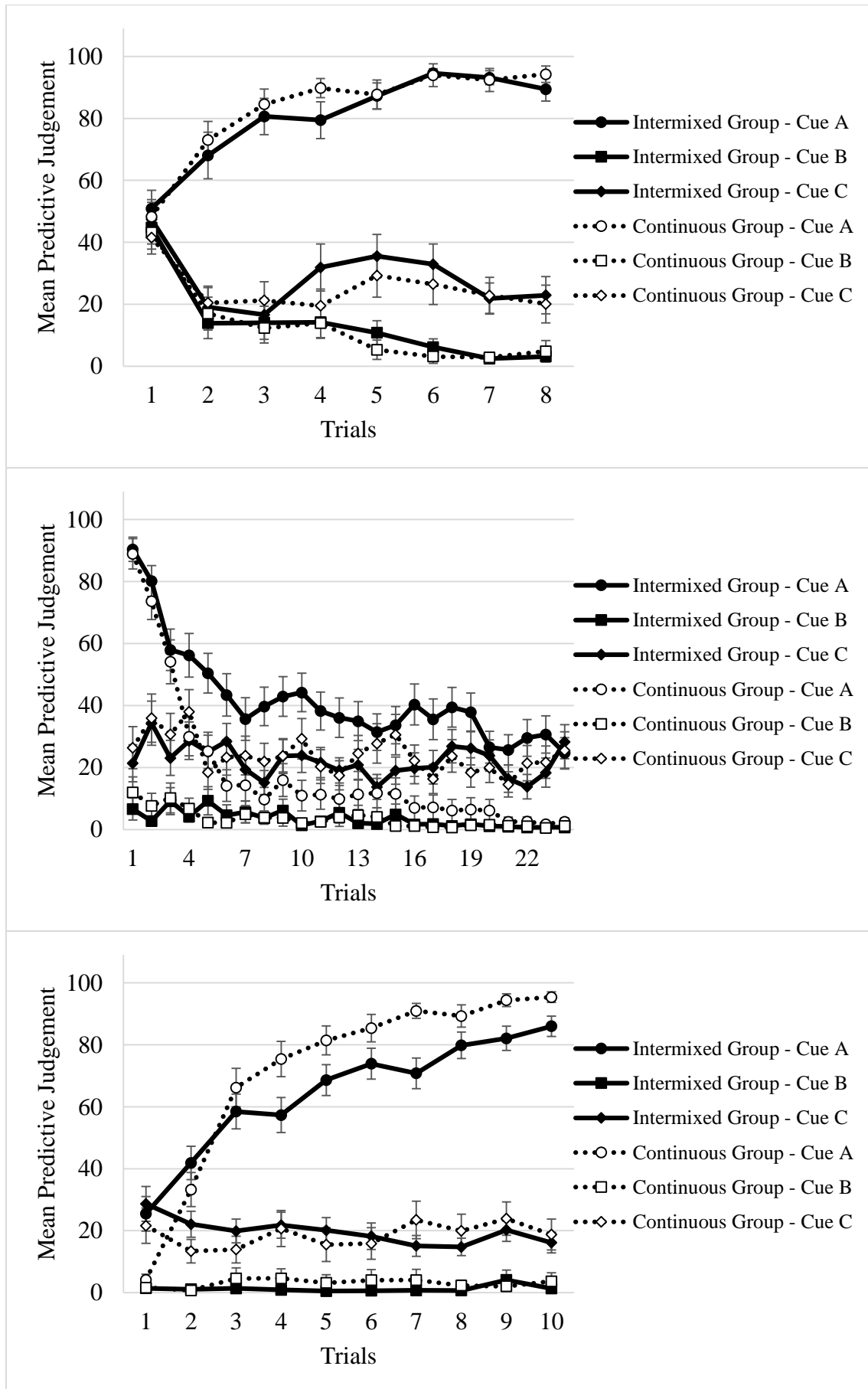


Figure #3

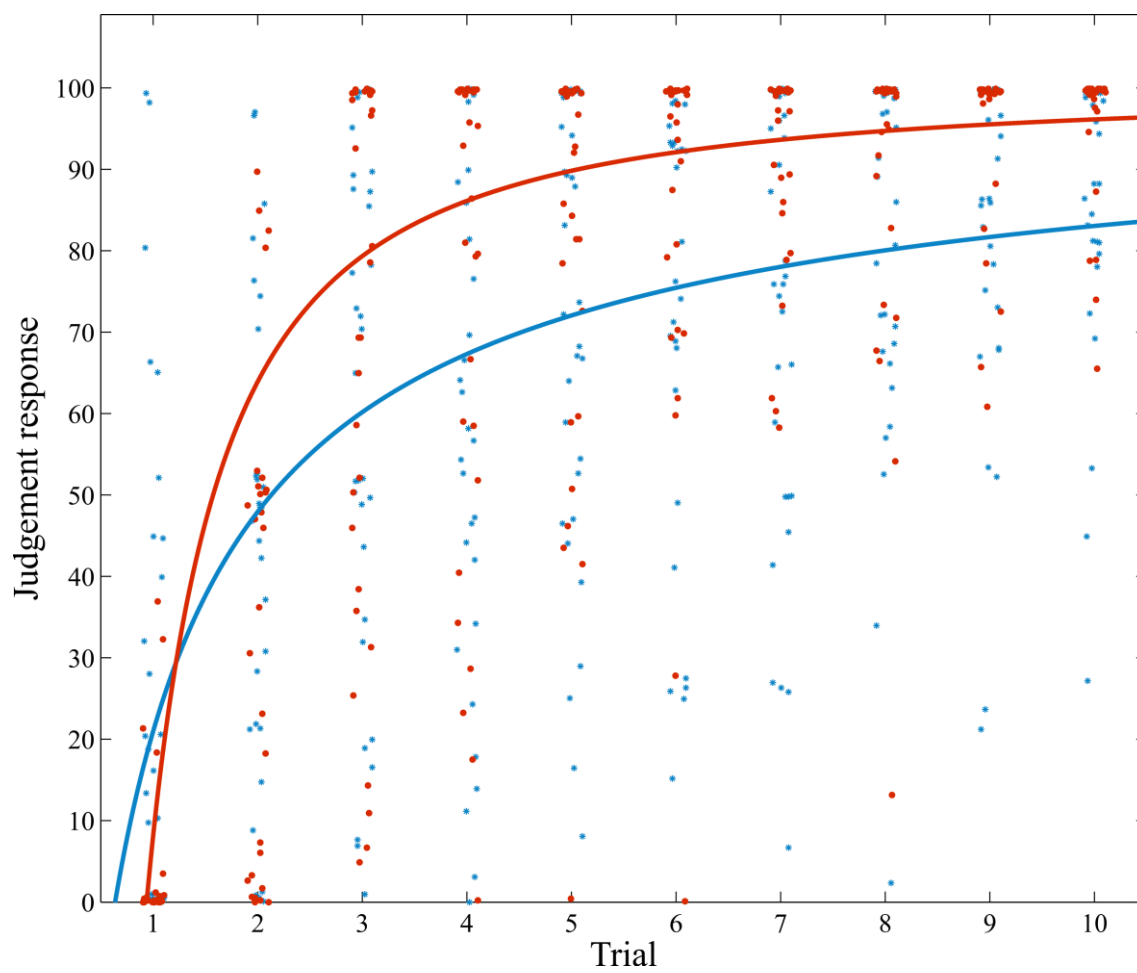


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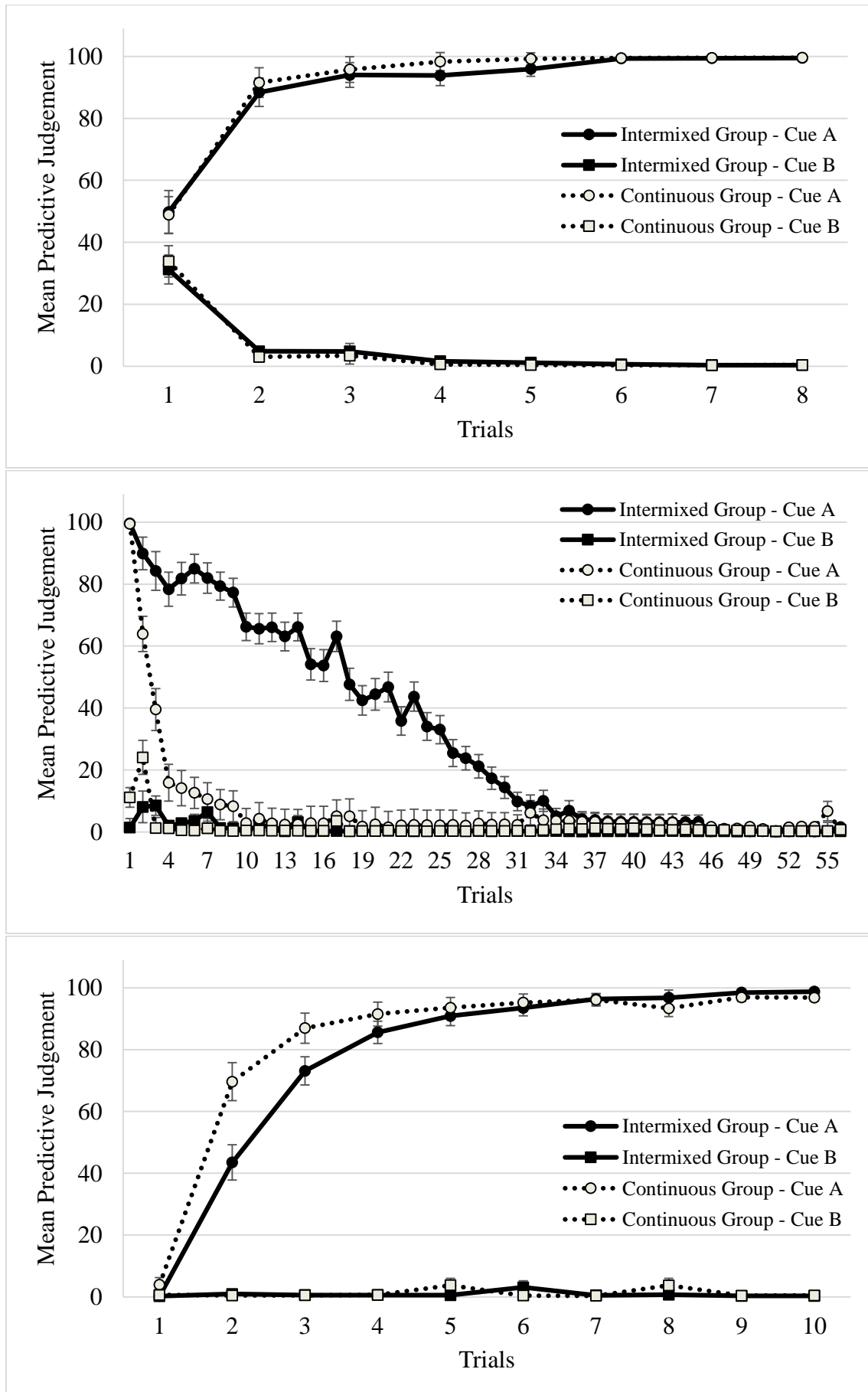


Figure #5

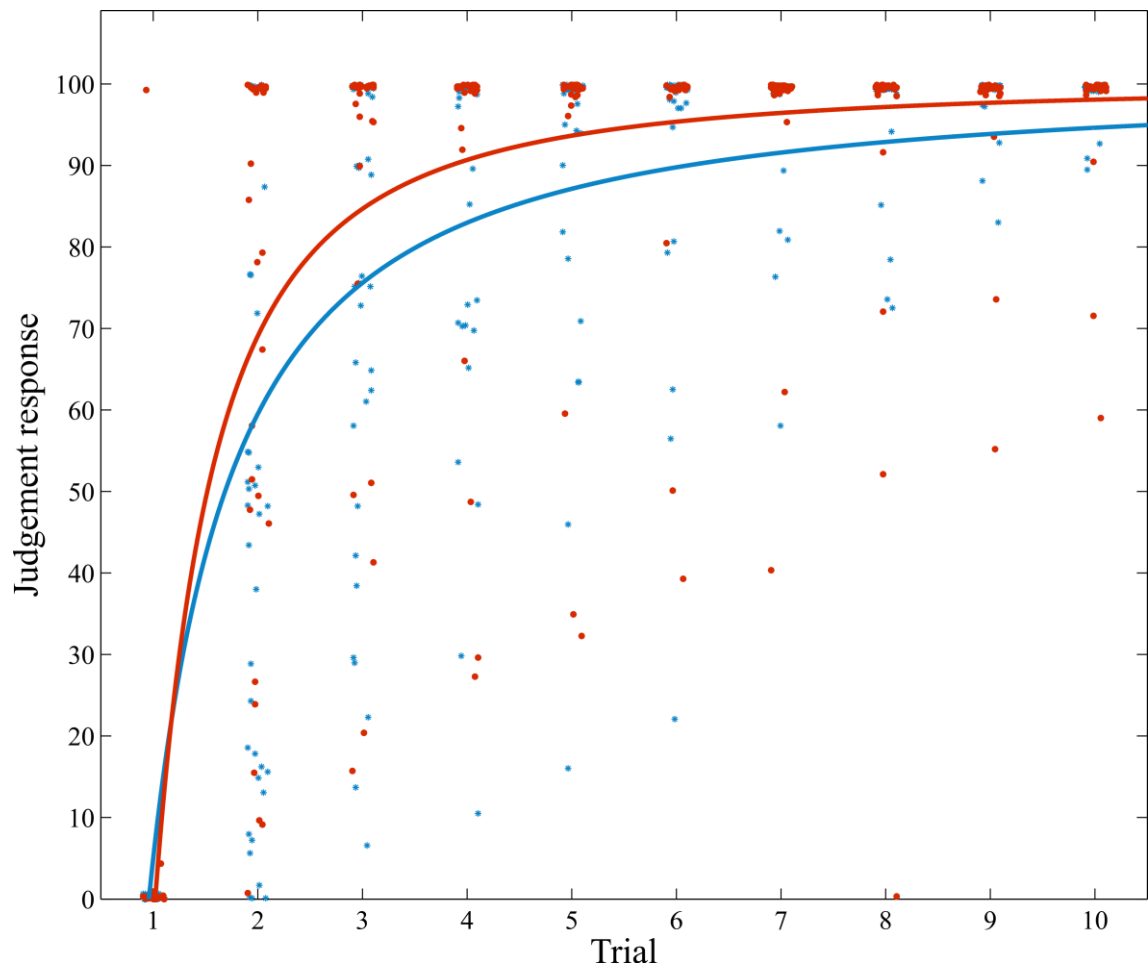


Figure #6